

We claim:

1. An isolated or purified modified erythropoietin construct (MEC) from the group consisting of:
 - a) SEQ ID NO: 10;
 - b) SEQ ID NO: 11;
 - c) SEQ ID NO: 12;
 - d) SEQ ID NO: 13;
 - e) SEQ ID NO: 14; and
 - f) truncated modified erythropoietin constructs of lengths X to Y, wherein X is an integer selected from 1, 2, 3, 4, 5, or 6 and Y is an integer selected from 188, 189, 190, 191, 192, or 193.
2. The isolated or purified modified erythropoietin construct according to claim 1, further comprising a heterologous polypeptide sequence.
3. A composition comprising an isolated or purified modified erythropoietin construct of claim 1 or 2 and a carrier or diluent.
4. An isolated, purified, or recombinant nucleic acid encoding a MEC according to claim 1 or 2.
5. The isolated, purified, or recombinant nucleic acid of claim 4, further comprising regulatory elements, vector elements, or other nucleic acid elements.
6. A host cell transformed with an isolated nucleic acid according to claim 4 or 5.
7. An isolated, purified or recombinant polynucleotide sequence comprising:

a) a sequence encoding a polypeptide sequence selected from the group consisting of SEQ ID NO: 10, 11, 12, 13, 14, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, and 244;

b) a complementary polynucleotide sequence to a polynucleotide sequence encoding a polypeptide sequence selected from the group consisting of SEQ ID NO: 10, 11, 12, 13, 14, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, and 244;

c) a polynucleotide sequence having at least about 20% to 99.99% identity to a polynucleotide sequence of (a) or (b); or

a fragment of a polynucleotide sequence according to (a) or (b).

8. A peptide, polypeptide, protein, or antibody having reduced immunogenicity as compared to the naturally occurring form of the peptide, polypeptide, or protein while retaining at least 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, or 100% of the biological activity of the unmodified or naturally occurring molecule and said reduced immunogenicity is the result of reduced binding to MHC Class II molecules.

9. The peptide, polypeptide, or protein according to claim 8, wherein the peptide, polypeptide, or protein is a therapeutic peptide, polypeptide, protein or antibody used in the diagnosis or treatment of diseases, conditions, or disorders.

10. The peptide, polypeptide, protein, or antibody according to claim 8 or claim 3, wherein peptide, polypeptide, or protein comprises all, or a portion of, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-15, IL-16, IL-18, IL-19, IL-23, IL-24, erythropoietin (EPO), insulin, human growth hormone, calcitonin, Factor VIII, G-CSF, M-CSF, GM-CSF platelet derived growth factor (PDGF), MSF, FLT-3 ligand, EGF, fibroblast growth factor (FGF); human insulin alpha, human insulin beta, insulin-like growth factors; vascular endothelial growth factor (VEGF); interferons; leukemia inhibitory factor (LIF); ciliary neurotrophic factor (CNTF); oncostatin M; stem cell factor (SCF); transforming growth factors; chemokines, or antibodies selected from the group consisting of REMICADE® (Infliximab); REOPRO® (Abciximab); SIMULECT® (Basiliximab); ZENAPAX® (Daclizumab); HERCEPTIN® (Trastuzumab); SYNAGIS® (Palivizumab); and XOLAIR® (Omalizumab).

11. The peptide, polypeptide, protein or antibody according to claim 10, wherein the protein is EPO and comprises a sequence selected from the group consisting of SEQ ID NOs: 10, 11, 12, 13, 14, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174,

175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, and 244.

12. An isolated, purified, or recombinant erythropoietin (EPO) polypeptide containing a substituted peptide segment, wherein said substituted peptide segment is located at positions G101-Q115 (SEQ ID NO: 40) or D136-R150 (SEQ ID NO: 47), and said substituted peptide segment contains at least one amino acid substitution.

13. The isolated protein of claim 11, comprising an amino acid sequence selected from the group consisting of: SEQ ID NO:10; SEQ ID NO:11; SEQ ID NO:12; SEQ ID NO:13; SEQ ID NO:14; SEQ ID NO:152; SEQ ID NO:154; SEQ ID NO:155; SEQ ID NO:159; SEQ ID NO:162; SEQ ID NO:181; SEQ ID NO:187; SEQ ID NO:199; SEQ ID NO:225; SEQ ID NO:226; SEQ ID NO:227; SEQ ID NO:228; SEQ ID NO:229; and SEQ ID NO:233; SEQ ID NO:245; SEQ ID NO:246; and SEQ ID NO:247.

14. A composition comprising a peptide, polypeptide, protein, or antibody according to claims 8, 9, 10, 11, 12, or 13 and a carrier or pharmaceutically acceptable excipient.

15. A method of antagonizing an EPO receptor or a method of treating diseases or conditions associated with over-activation of the EPO receptor comprising the administration of a composition comprising the EPO variant SEQ of non-activating EPO in amounts sufficient to: 1) block the binding of naturally occurring EPO to its receptor; or 2) reduce the activation levels of the EPO receptor.

16. An isolated, purified, or recombinant polynucleotide encoding a peptide, polypeptide, protein and/or antibody according to claims 8, 9, 10, 11, 12, or 13.

17. An isolated, purified, or recombinant polynucleotide according to claim 16, further comprising regulatory elements selected from promoters, enhancers, termination sequences, and combinations thereof.

18. A vector comprising an isolated, purified, or recombinant polynucleotide according to claims 16 or 17.

19. A host cell comprising an isolated, purified, or recombinant polynucleotide according to claims 16, 17 or 18.

20. A method of producing a recombinant peptide, polypeptide, protein or antibody comprising the culturing of a host cell according to claim 19 under conditions that allow for the expression of a recombinant peptide, polypeptide, protein or antibody.

21. The method according to claim 20, further comprising the isolation of the recombinant peptide, polypeptide, protein and/or antibody from the host cell or culture system.

22. A method for reducing a helper T lymphocyte (HTL) response against a candidate protein comprising: a. selecting a protein; b. analyzing the amino acid sequence of the protein for potential HTL epitopes; and c. modifying the amino acid sequence of the protein by removing the potential HTL epitope and thereby generating an analog protein.

23. The method according to claim 22, further comprising conducting in vitro antigenicity analysis of said candidate protein using helper T-cells.

24. The isolated, purified, or recombinant EPO polypeptide of claim 12, wherein said EPO polypeptide contains substituted peptide segments at positions G101-Q115 (SEQ ID NO: 40) and D136-R150 (SEQ ID NO: 47).

25. The isolated, purified, or recombinant EPO polypeptide of claims 12 or 24, wherein said peptide segments are selected from those peptides set forth in Tables 10A, 10B, 11A, 11B, 12, 13A, 13B, 14A, 14B, or 14C.

26. The isolated, purified, or recombinant EPO polypeptide of claims 12 or 24, wherein said peptide segment is selected from the group consisting of: SEQ ID NO:152; SEQ ID NO:154; SEQ ID NO:155; SEQ ID NO:159; SEQ ID NO:162; SEQ ID NO:181; SEQ ID NO:187; SEQ ID NO:199; SEQ ID NO:225; SEQ ID NO:226; SEQ ID NO:227; SEQ ID NO:228; SEQ ID NO:229; and SEQ ID NO:233; SEQ ID NO:245; SEQ ID NO:246; and SEQ ID NO:247.